UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/674,516 | 09/30/2003 | Sridevi Dhanaraj | 1264-15 | 5523 |

23869 7590 06/19/2006

HOFFMANN & BARON, LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

| EXAMINER | |
|---|---|
| RUSSEL, JEFFREY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1654 | |

DATE MAILED: 06/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/674,516 | DHANARAJ ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey E. Russel | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *58* is/are withdrawn from consideration.

5)☒ Claim(s) *59* is/are allowed.

6)☒ Claim(s) *1,4-31,33-36,38-52,54 and 56* is/are rejected.

7)☒ Claim(s) *2,3,32,37,53,55 and 57* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20031201;20050620*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-57 and 59, drawn to a composition comprising a peptide and methods of use, classified in class 514, subclass 16.

II. Claim 58, drawn to DNA encoding a species of the peptide, classified in class 536, subclass 23.1.

The inventions are independent or distinct, each from the other because:

Inventions I and II are directed to related products. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the peptides and the DNA do not overlap in scope and are mutually exclusive. There is no significant common structure or function between peptides and DNA encoding the peptides. The peptides and DNA are not capable of use together and are used for materially different purposes, i.e. the peptides are used therapeutically whereas the DNA is used to synthesize the peptides.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

During a telephone conversation with Attorney Gloria K. Szakiel on May 9, 2006, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-57 and 59. Affirmation of this election must be made by applicant in replying to this Office action. Claim 58 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. The Sequence Listing filed May 5, 2005 is approved.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or

absence of working examples; and (8) the quantity of experimentation necessary. With respect to (1), the nature of the invention is a method for promoting the proliferation and/or differentiation of mesenchymal stem cells using a peptide component of formula (I). With respect to (2), the state of the prior art is relatively undeveloped. As summarized by the Fibbe article (Ann. Rheum. Dis. Vol. 61, Suppl. II, pages ii29-ii31), "A number of fundamental questions relating to the biology of MSCs are still unanswered." Among these questions, the Fibbe article includes the role of microenvironment in differentiation and development. See page ii30, column 2, last paragraph. The prior art of record does not disclose the use of peptides of Formula (I), or of any compounds which are structurally related to these peptides, to promote the proliferation and/or differentiation of mesenchymal stem cells. Compare, e.g., the stimuli listed in Table III of the Minguell et al article (Exp. Biol. Med., Vol. 226, pages 507-520). With respect to (3), the relative skill of those in the art is high. With respect to (4), the predictability of the pharmaceutical art is relatively low. One skilled in the art in general can not predict the activity of a compound, including peptides, in the absence of some type of testing. With respect to (5), the claims are relatively narrow in scope, reciting a relatively narrow range of peptides and requiring a relatively specific result, i.e. promoting the proliferation and/or differentiation of mesenchymal stem cells. With respect to (6) and (7), no direction or guidance is given as to how the peptides of formula (I) can be used to promote the proliferation and/or differentiation of mesenchymal stem cells. There are no working examples, ex vivo, in vivo, in vitro, or otherwise, in which peptides of Formula (I) are used to promote the proliferation and/or differentiation of mesenchymal stem cells. With respect to (8), the quantity of experimentation necessary to use the invention would be relatively large, given the relatively undeveloped state of

the prior art and given the lack of any working examples in the disclosure. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

4. Claims 1, 4-31, 33-36, 38-52, 54, and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The independent claims recite a "derivative" of peptides of Formula (I); however, "derivative" is not defined in the disclosure or the art. It is not clear what degree of similarity, structural or functional or otherwise, a compound must have with a peptide of Formula (I) in order to be considered a "derivative" and therefore embraced within the scope of the claims.

5. Claims 1, 4-31, 33-36, 38-52, 54, and 56 are objected to because of the following informalities: At claim 1, lines 7 and 10, "a" should be changed to "the"; and at lines 8 (second occurrence) and 11 (second occurrence), "or" should be changed to "the"; so that standard Markush terminology is used. These same changes should be made to independent claims 30, 36, 50, 54, and 56. At claim 27, line 4-5, "copolymers of polyurethane and poly(lactic acid)" is repeated, and one of the two occurrences should be deleted. At claim 27, line 5, the beginning parenthesis before "poly(lactic acid)" (first occurrence) should be deleted. Appropriate correction is required.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

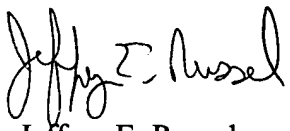
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 30, 36, 50, 54, and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Dee et al (U.S. Patent No. 6,262,017). Dee et al teach peptides of the formulas recited in claims 1 and 2 immobilized on a substrate. The immobilized peptides are implanted in vivo and used as a bone prosthetic device. The peptides result in enhanced osteoblast adhesion to the implants. See e.g., the Abstract and the claims. The peptides of Dee et al correspond to the derivative recited in Applicants' claims, in view of the amino acids in common between the peptides of Dee et al and the peptides of Formula (I) recited in Applicants' claims (for example, SEQ ID NO:4 of Dee et al comprises three contiguous glycine residues, as does Applicants' SEQ ID NO:1) and in view of their similarity in function and use (both are used as bone implant materials). Note that Applicants have not defined "derivative" so as to require any particular degree of structural and/or functional similarity between the derivative and the peptide of formula (I) (see also the rejection under 35 U.S.C. 112, second paragraph, set forth above).

8. Claim 59 is allowed. Claims 2, 3, 32, 37, 53, 55, and 57 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art of record does not teach or fairly suggest compounds comprising the structure of Formula (I), including compounds comprising SEQ ID NO:1, or pharmaceutically acceptable salts thereof. Accordingly, compositions and kits comprising these compounds, and methods of using these compounds, are also novel and unobvious over the prior art of record. If the independent claims were to be re-written so as to delete the "derivative" language, then the rejection under 35 U.S.C. 112, second paragraph, and the anticipation rejection over Dee et al (U.S. Patent No. 6,262,017) would be withdrawn.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

June 14, 2006